REQUEST FOR INFORMATION: DESIGN AND IMPLEMENTATION OF A LARGE-SCALE PROSPECTIVE COHORT STUDY OF GENETIC AND ENVIRONMENTAL INFLUENCES ON COMMON DISEASES

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National Institutes of Health (NIH)
(http://www.nih.gov/)

Response Due Date: May 28, 2004

BACKGROUND

The completion of the Human Genome Project provides an unprecedented opportunity to define the genetic and environmental contributions to health and disease. Well-designed, disease-specific case-control studies are critical to this effort, but rigorous and unbiased conclusions about disease etiology and population impact will require prospective population-representative designs. Replication of associations and estimation of their magnitude, consistency, and temporality (all key criteria for epidemiologic evidence of causal relationships), can only be obtained through prospective, population-based cohort studies. A large-scale prospective cohort study in the United States is a logical next step in the systematic elucidation of gene-environment-disease relationships.

Characteristics of such a study that might maximize its research value may include: 1) a sufficiently large number of participants to achieve adequate power for common disorders, particularly for gene by environment interactions; 2) intentional over-sampling of minority groups to permit meaningful inferences about these groups and to study health disparities; 3) a broad age range to provide information on disorders from infancy to old age; 4) a broad range of genetic backgrounds and environmental exposures; 5) family-based recruitment for at least a portion of the cohort to increase the power of genetic analyses and control for population stratification; 6) a broad array of clinical and laboratory information, not limited to any single disease; 7) sophisticated dietary, other lifestyle, and environmental exposure assessment; 8) collection and storage of biological specimens including DNA, plasma, and cells; 9) a highly sophisticated data management system; 10) free and open access to study data and biologic materials, to empower research on many diseases by researchers in many sectors; and 11) comprehensive community
engagement in the design and implementation of the study, including a state-of-the-art consent process to allow multiple uses of the data, regular feedback to participants about progress, and a study design that ensures a high follow-up rate.

Accordingly, the NIH is soliciting input from the scientific community and the public to guide in developing such a study.

PURPOSE

This request for information seeks advice on approaches to developing a large-scale U.S. study of genetic and environmental influences on common diseases. Advice could include recommendations on optimal characteristics of such a study, such as some of the items described above; recommendations on combining existing cohorts for such efforts; and characteristics of existing studies that might lend themselves to inclusion in such efforts. Respondents are asked to comment on one or more of the issues listed below (using the link to
the online form at the end of this document if possible) but should not feel compelled to address all issues.

INFORMATION REQUESTED

1. If appropriate funding were available to support a large cohort study (N ~ 500,000) of genetic and environmental determinants of major complex diseases, please comment on what you would see as advantages of recruiting and examining a new cohort vs. building upon existing cohorts.

2. Please describe the characteristics of a large US cohort study that you view as most important to include in any such effort that might be undertaken.

3. Please suggest the family structures, and proportion of related individuals, that you would recommend for inclusion in the proposed study.

4. Please identify the most relevant issues concerning the power to detect genetic effects (such as environmental risk factors, heterogeneity, prevalence) for diseases or traits that you would be interested in studying in a large US cohort study.

5. Other information not specifically addressed by the comments above, but considered important and relevant to the development and implementation of a large-scale study of genetic and environmental influences on common diseases, would also be of considerable interest and value.

If you are the investigator responsible for a prospective population-based study with stored DNA, please comment on the following considerations if existing cohorts were to be combined. Please feel free to illustrate with examples from your own research, experience and/or professional expertise.

6. How likely your study would be to participate in this effort and contribute data and genetic samples, and the main obstacles to your study’s participation.

7. How likely your study would be to make its data accessible for use and analysis by other researchers, and the main obstacles to your study allowing such access.

8. Please comment on what additional consent might be needed from your study participants, how it could be obtained, and how likely it might be that roughly 80% or more would consent.

9. Please comment on what additional phenotyping, primarily for diseases or risk factors other than those for which the study was established, might be possible in existing cohort studies such as yours.

10. Please suggest how participants might be selected for the proposed study and how that approach would compare to your own study, including roughly what proportion of those invited might agree to participate.

11. Please comment on the age, race, and sex distribution of existing cohorts such as yours, both at entry and likely to be available and participating in the proposed gene-environment study.

12. Please comment on the proportion of participants in existing cohorts such as yours likely to have stored DNA available for genotyping, and to have available other biologic materials such as serum, urine, other tissue, etc.

13. Please advise on how disease endpoints are identified in existing cohort studies such as yours (that is, through registries, medical records review, participant contact), how often participants are contacted, with roughly what retention rate, and how long follow-up is scheduled to continue.

14. Please comment on the proportion of participants in existing cohort studies such as yours related in the second degree or closer (that is, grandparents-grandchildren, half-siblings, aunt/uncle-niece/nephew).

Responses in any of the 14 areas are welcome; respondents should not feel compelled to address all 14 issues. Responses will be compiled and shared with advisory committees involved in the development and approval of this study concept. Should the responses be shared with other individuals, the names of the respondents will be witheld.

We look forward to your input and hope you will share this document with your colleagues. Thank you very much for your help.

To respond, please link to the online form at
http://grants.nih.gov/cfdocs/rfi_not-od-04-041/rfi_form.htm,
or send a letter, fax or email to the following address:

Teri Manolio, M.D., Ph.D.
6701 Rockledge Drive

Room 8160, MSC 7934
Bethesda, Maryland 20892-7934
FAX (301) 480-1667
Phone (301) 435-0708
Email: NHLBI_CohortStudy@mail.nih.gov

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Department of Health
and Human Services

National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892